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U.S. ARMY MEDICAL RESEARCH & NUTRITION LABORATORY

INFLUENCE OF ORALLY ADMINISTERED
ANTIBIOTICS ON GROWTH AND
PLASMA LIPID LEVELS OF GROWING CHICKS

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Report No. 276

12 March 1963

Report of

INFLUENCE OF GRALLY ADMINISTERED ANTIBIOTICS ON GROWTH AND PLASMA LIPID LEVELS OF GROWING CHICKS

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Subproject No. 2, Workphase 24

INFLUENCE OF ORALLY ADMINISTERED ANTIBIOTICS ON GROWTH AND PLASMA LIPID LEVELS OF GROWING CHICKS

OBJECT:

To determine the influence of orally administered antibiotics on plasma lipids of growing chicks.

SUMMARY:

Growing chicks were fed semi-purified diets supplemented with antibiotics or sulfa drugs in the presence or absence of supplemental cholesterol.

The data indicate that antibiotics and sulfa drugs depress plasma cholesterol levels of chicks fed a cholesterol-free diet when they also stimulate growth, but are without effect in the absence of such a growth stimulation. In cholesterol-fed chicks, antibiotics and sulfasuridine elevated plasma cholesterol and lipid phosphorus levels.

A highly significant positive correlation was observed between plasma cholesterol and lipid phosphorus levels for chicks for either a cholesterol-free or supplemented diet.

APPROVED:

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Director

INTRODUCTION

Recent studies have demonstrated an effect of dietary antibiotics on serum cholesterol levels. Nelson et al. (9) observed that the addition of chlortetracycline to a commercial ration resulted in increased serum cholesterol and lipids in rabbits. Goldberg and Smith (1), employing a low-fat and a 12.5% cottonseed oil diet, reported that chlortetracycline resulted in a slight increase in the plasma cholesterol level of rabbits receiving the low-fat diet as compared to a decrease in serum and tissue cholesterol of animals receiving the cottonseed oil ration.

The type of carbohydrate fed also appears to influence the effect of antibiotics and sulfa drugs on serum cholesterol levels. Portman et al. (10) reported that succentylsulfathiazole did not alter the serum cholesterol of rats receiving a sucrose diet, but elevated the serum cholesterol levels of rats fed a starch-containing diet. Kritchevsky et al. (5) found elevated cholesterol levels in chicks fed cholesterol when the diet contained glucose as the carbohydrate source, but not when sucrose replaced glucose.

Recently, Howe and Bossharit (3, 4) have studied the effect of oxytetracycline, chlortetracycline and succinylsulfathiazole on plasma cholesterol in the mouse. These authors found an elevation in plasma cholesterol when oxytetracycline and succinylsulfathiazole were fed in a diet containing saturated fat, cholesterol and cholic acid. When an unsaturated fat replaced the saturated fat, oxytetracycline was without effect. Chlortetracycline under similar conditions depressed plasma cholesterol. In diets without added cholesterol, chlortetracycline produced lowered cholesterol levels only in the presence of highly unsaturated fat such as cod liver oil and had no effect in the presence of less highly unsaturated fats such as corn oil.

In human subjects, Samuel and Steiner (12) reported a hypocholesteremic effect for necmycin. More recently, Steiner et al. (13) have shown that intramuscularly administered necmycin failed to influence serum cholesterol levels in athemseleratic patients, and concluded that oral necmycin depresses serum cholesterol through a local effect on the gastrointestinal tract. The hypocholesterolemic effect of oral necmycin has been corresponded (11) and evidence has been presented which indicates that the effect of necmycin is mediated by impairing lipid absorption (8).

The data to be presented indicate that plasma cholesterol levels of growing chicks are not influenced by antibiotics except in situations where they also have a growth-stimulating effect.

EXPERIMENTAL

Male Hy-Lire chicks were used in two experiments. The chicks were fed a commercial diet for one week prior to receiving the experimental diets. The experimental period was of three weeks' duration in experiment I and four weeks in experiment II.

The chicks were housed in heated cages having raised wire floors. The composition of the basal diet used for both experiments is shown in Table 1; the design of each experiment is indicated in the tables of results (Tables 2 and 3).

At the termination of the experimental period, blood samples were obtained by cardiac puncture using heparin as an anticoagulant. The blood was centrifuged and the plasma taken for cholesterol, and in experiment II, for lipid phosphorus analysis. Cholesterol and lipid phosphorus were determined by previously described procedures (7).

RESULTS

All the antibiotics fed in experiment I with the exception of oxytetracycline stimulated growth significantly (Table 2); oxytetracycline also stimulated growth, but the difference was not statistically significant. All the treatments employed did, however, significantly depress plasma cholesterol levels.

In experiment II, penicillin, name on and sulfasuridine did not influence growth or plasma lipid levels of chicks fed a cholesterolfree diet. In the cholesterol-supplemented groups, however, growth was depressed by neomyoin and sulfasuridine, and plasma cholesterol and lipid phosphorus were elevated by all treatments.

In Figures 1 and 2 are presented the relationship between plasma cholesterol and lipid phosphorus of chicks fed a cholesterol-free and supplemented diet, respectively. In both cases, a highly significant (P < 0.01) correlation between these parameters was observed, the correlation coefficients being + 0.68 and + 0.88 for the cholesterol-unsupplemented and supplemented groups, respectively.

DISCUSSION

The results obtained in the two experiments for chicks fed a cholesterol-free diet are not in agreement. In experiment I, antibiotics depressed plasma cholesterol while in experiment II they were ineffective. The response in experiment I can probably be related to the growth stimulation. It has been demonstrated previously that low-protein diets and smine acti-deficient diets

which depress growth also elevate plasma chclesterol (7). The growth-stimulating effects of antibiotics are generally only evident in animals housed in unclean quarters or suffering from subclinical infections (2). The growth stimulation resulting from antibiotic feeding in experiment I might very well indicate the presence of such a mild infection which was absent in experiment II.

The hypercholesterolemic effect of the antibiotics and sulfa drug fed in experiment II is in accord with findings in cholesterol-fed rabbits (9). The effect of neomycin is in contrast to its hypocholesterolemic effect in the human (12). Further studies are necessary to gain a better understanding of the mechanism of action of antibiotics in altering blood lipids.

The correlation observed between plasma cholesterol and lipid phosphorus levels is in accord with a previous report (6). These data show a much slower increase in the cholesterol:phospholipid ratio with increasing plasma cholesterol levels in chicks fed the cholesterol-free diet than in the cholesterol-fed chick. The increase in lipid phosphorus accompanying plasma cholesterol levels can be interpreted to represent a homeostatic mechanism which the animal appears capable of maintaining in an endogenous hypercholesterolemia. However, in an exogenous hypercholesterolemia resulting from cholesterol feeding, the increase in cholesterol level is so great and rapid that the animal cannot maintain the constancy of the cholesterol: lipid phosphorus ratio.

ACKNOWLEDGMENTS

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TABLE 1
Composition of Basal Diet

Ingredient	gm/100 gm diet
Yellow corn meal	34.26
Soybean oil meal	30.84
DL-methionine	0.30
Corn oil	3.00
Salt mixture	4.00
Vitamin mixture ²	0.40
Choline Cl	C.20
Glucose	to 100.00
•	

l Chick salt mixture, supplied per kg of diet when fed at the rate of 5.31% of the diet: (in grams) CaCO3, 3.0; Ca3(PO4)2, 28.0; K2HFO4, 9.0; MgSO4, 1.25; Fe gluconate, 2.24; NaCl, 8.80; and (in milligrams) ZnSO4.7H2O, 60; KI, 40; CuSO4, 20; H3BO3, 9; CoSO4.7H2O, 1; MnSO4, 650.

² Chick vitamin mix, supplied in mg/kg of diet when fed at the rate of 0.40% of the diet; thiamine.HCl, 25.0; riboflavin, 16.0; Ca pantothenate, 20.0; pyridoxine, 6.0; bictin, 0.6; folic acid, 4.0; p-aminobenzoic acid, 2.0; menadione, 5.0; and vitamin B_{12} , 20 µg; inositol, 100; ascorbic acid, 250; niscin, 150; vitamin A, 10,000 IU; vitamin D_3 , 1,000 ICU; a-tocopheryl acetate, 100 mg.

TABLE 2

Influence of Orally Administered Antibiotics on Weight Gain and Plasma Cholesterol Level of Chicks

		Exg	Experiment I		
Supplement	Level fed	Body weight gain	P value ² compared to control	Plasms cholesterol	P value ² compared to control
	per kg of diet	5.		mg/100 ml	
None		226 ± 16 ³		164 ± 253	
Penicillin G	2,000 units	247 ± 25	< 0.05	112 ± 15	6.0
Oxytetracycline. HCl	300 years	243 ± 36	NB ²	126 ± 15	< 0.01
Chlortetracycline	100 year	æ ∓ 99e	©.0 ➤	123 ± 18	CO.O
Neomycin SO4	2.0 mg	256 ± 32	< 0.02	141 + 15	<0.05
Succinylsulfsthiszole	e 10 gm	264 ± 25	™.o>	140 ± 15	< 0.02

¹ Weight guin from 7th to 28th day of age.

² Probability (P) of values being different from unsupplemented control group; P>0.05 taken as not significant (NS).

³ Mean for 10 chicks # standard deviation.

TABLE 3

Influence of Orally Administered Antibiotics on Weight Cain and Plasma Lipids of Chicks Fed Diets Containing or Free of Cholesterol

Experiment II

5.	Body weight gain- gm P value3	Plasma cholesterol mg/100 ml P value3	terol value3	Flasma lipid phosphorus mg/loo ml P value	hosphorus P value 3
	No add	No added cholesterol	TX.		
+++	4 0.01 NS	176 ± 21 ⁴ 190 ± 26 187 ± 30	NS NS	13.3 ± 1.3 ⁴ 13.4 ± 2.6 11.7 ± 2.4	SN SN SN
41	NS	185 ± 17		14.0 ± 1.2	SN
	र्म हैं	olesterol adde	쩟		
##	NS	##	< 0.05	11.6 ± 1.7	₹ 0.01
44 44	~0.0 ~0.0	##	<0.02 NS	15.8 ± 2.3 17.9 ± 1.9	∨∨ 6.9.9
	317	# 27 ⁴	# 27 ⁴	# 27 ⁴	# 27 ⁴

l Penicillin G and neomycin SO4 were added at a level of 0.1% of the diet and sulfasuxidine at the 1% level.

² Weight gain from the 7th to the 35th day of age.

³ Probability of value being different from respective unsupplemented control group, P greaterfoan 0.05 taken as not significant (MS).

h Mesn for eight chicks & standard devistion.

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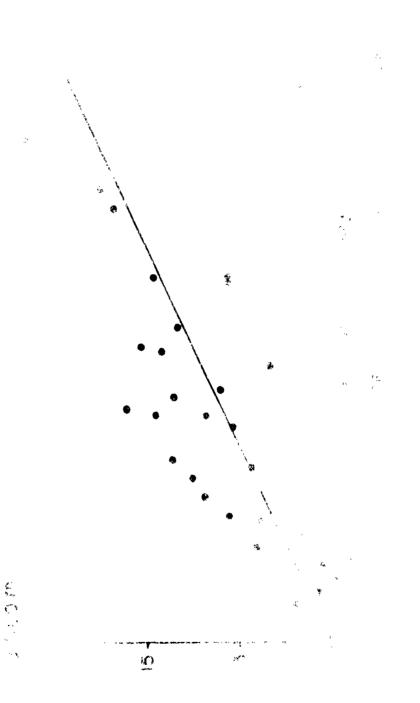
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